

Figure 1

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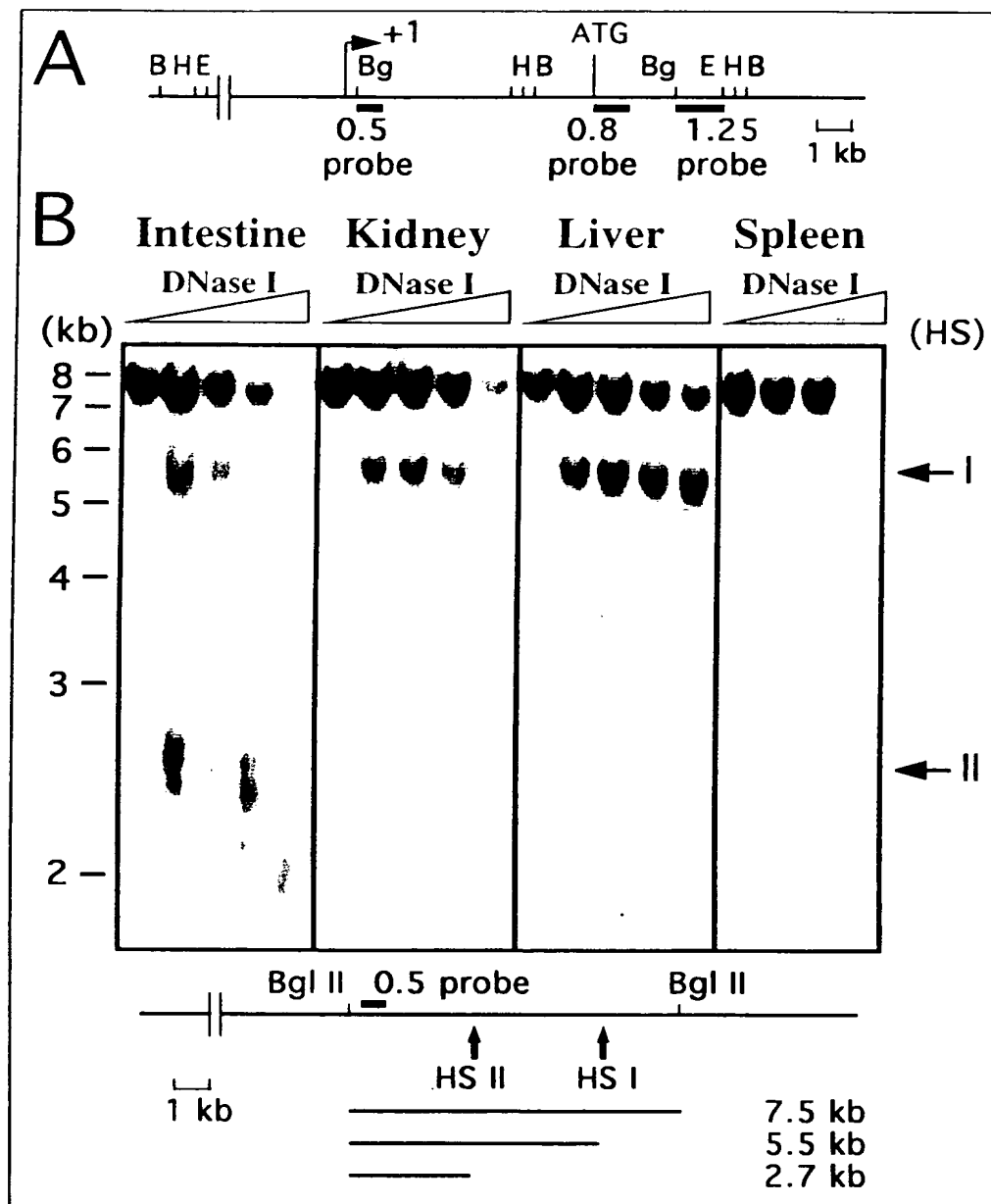


Figure 2 (a)

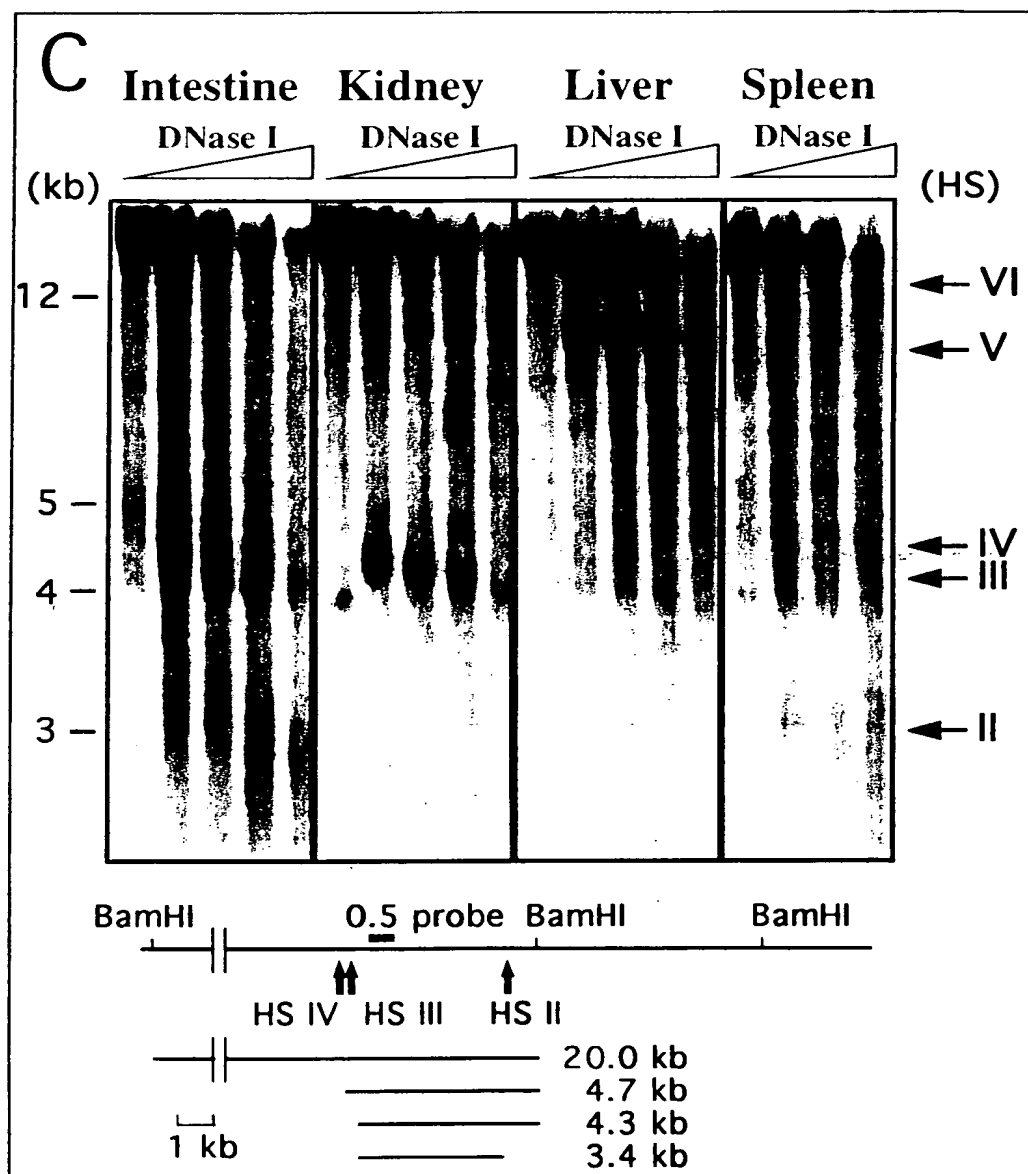


Figure 2 (b)

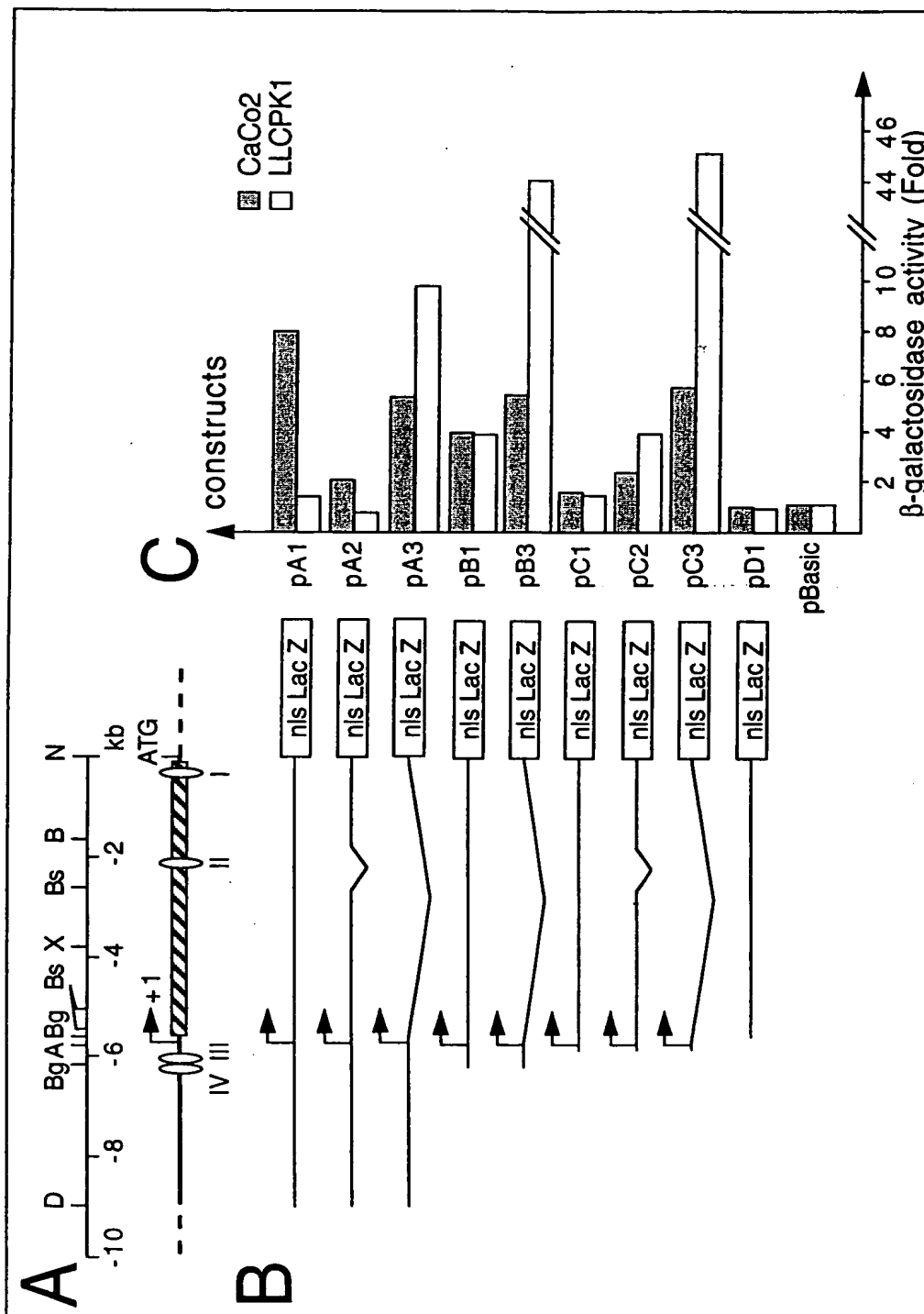


Figure 3

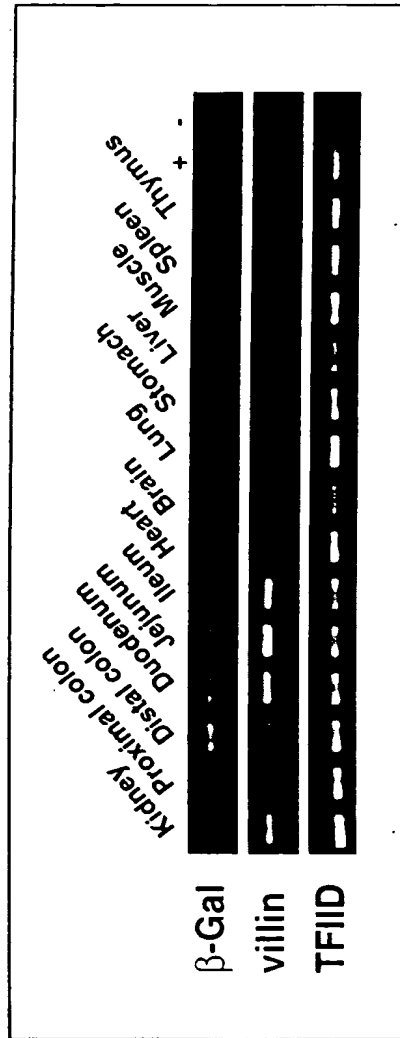


Figure 4

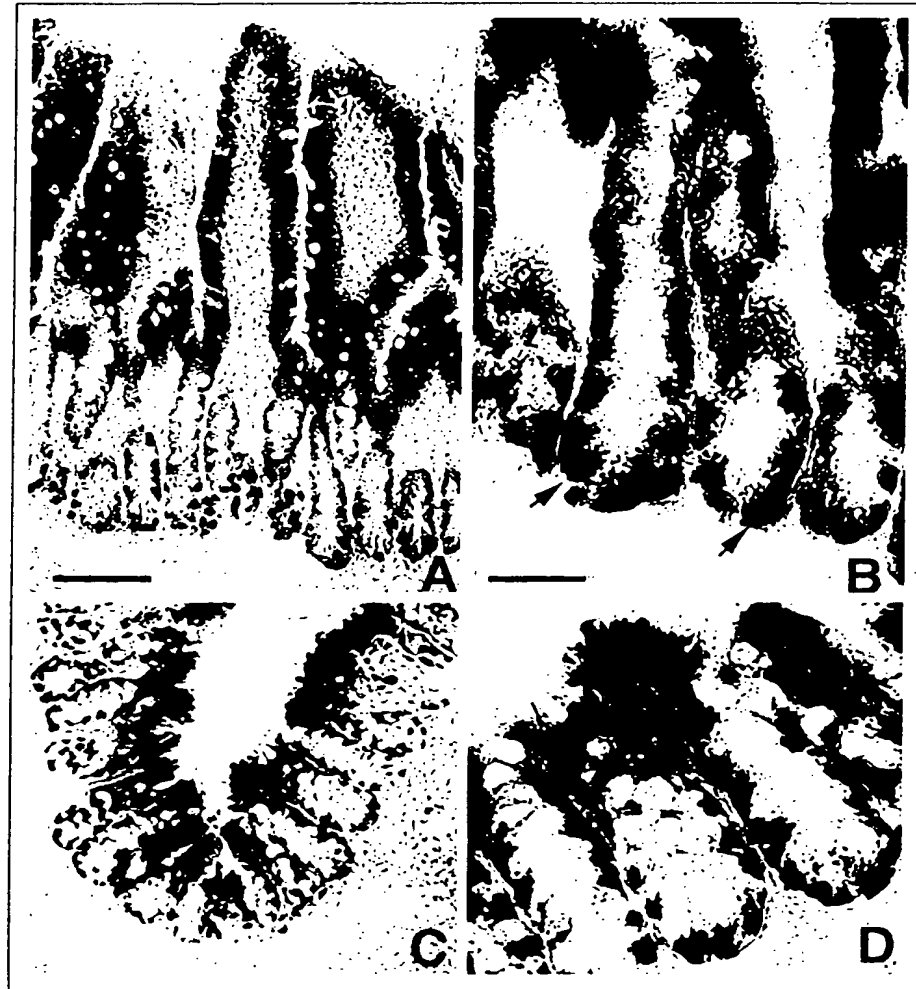


Figure 5

Genomic sequences of the mouse villin gene regulatory sequences

GATCTGGTGC ACCAAGGACA CTGTGGTCCC AGCACTGGGG AGGTGGAGGG AGGAGGGTCA 60
 GAAGTTTAAG GTCATCCTTG GTTACATAGC AAGGTTTCAG CCAGCTTCAG CTACATGAAA 120
 CCTTTGTTTG TTTGTTTGTT TGTTTTAAAG CATTAAATAA TAATACCATA AGGAGGTTGG 180
 CAGTGGTGGC AGACACCTTT AATTCCAGTA TTCAGGAGGC AGAAGCAGGC AGATCTCTGT 240
 GAGTTCGAAG TCAGCCTAGT CTGCAAAGCT AGTTCAGGA TGGCAAGGGC TACACAGAGA 300
 AACCTTGCTCT CATAAAACCA AAGTAGTAGT AGTAGTAGTA ATGCCATAGA GAAATTGGA 360
 GTCCATTTCAG GATGGACCAT CCTATAAGAT GATTCTCTTG ACCCAGGTAA GCTAATGTCA 420
 TGGGGAAAGG GGATGGGACT GTCCTAGATT AAAAAGTGCT GAGGCGATGC CTATTCTCAA 480
 TTTGATTCCA TATGAAAAGG CTGATAAGGC CCAAGAGAAG TGGAACTGGG ACTCTGGACT 540
 GAAGACGTGA CGGCCTTATA AACACTGGCA CTTATAAACA CTTATAAACA CTGGCACAGG 600
 CGTTCAGGTT TGAAGATCAC TTTCAAACCA CAGAACAGAA AGTGCTCGCT CGTCCTCAGC 660
 GTAGCGAGCA CTGGCTGCAG AAGAGTGATA TTTAGTGAAA GCTACCTTCA CAATATCTTT 720
 GCACTTATCA CATAACGTG TCAAATGTGC TAACTCCCTA GTCCACAGAT GGCTGTTACA 780
 CTCGTTTCTG CTTTCCCATC TGGTTGACAT TTGTCAGAAC CAGAAATTAG AAATGTGGGT 840
 ATTTATTTGT GTGCTGAGGA CACCATCCAG GGCTTTTCAC ATTTTCAGGCA CATGGTTTAC 900
 TAACTGGGCT ACTTCTCCAA CGGTTTGAAA CCATTTGTTT TATATTTACT TATTTTGTGT 960
 GCATGAGGTA GGCATGTATA CGTATGTATA GGAGTCATGC ATGTGGCTGC TACCCTCAA 1020
 ATCATTGCAG ATCCCAGCA AGTGAAGTCA CCGAGCGTTG TAAGTTGTTA TGTGGGACTG 1080
 GGAGCCAAGG CTGGGTTCCTC TGCAAGAGCA GCCAGTGGCC TTAACCATGG GACCAGCTCT 1140
 CTAGGCCTAA GGTAATCTTT AGTTTTTTAA AAATATATAT TCTCAGCCGG GTGTGGTGGC 1200
 ACACGCCTTT AATCCCAGCA CTTGAGAGGC TGAGGTGTAG GAATTATACA CACAGGCCAG 1260
 CTGGGGTGCA GAGCTTGGCC CTGTTTTTTT TGTTTTTTCT TTATGTGCAC TGGTGTCTTA 1320
 CCTGCGTGTA TGTCCGTGCA AGGGTGTGAG ATCCCTTGGA GCTGGAGTTA AAGACAGTTG 1380
 TGATCACGCT GCCGTTACAG ATGCTGGAAA TTGAACCCAG GTGTCCCTAG AGAAGCAGCC 1440
 AGTGCTCTTA ACTTCTGAGC CACCCCTCCA ACCCTGCTTT TAGAGACTCT TAACCTTTTG 1500
 TGTAATGTGG GAACTGAGTG GATCTTGAC TTACCAAGTG TGTGCTGCGC TGTAGCATCA 1560
 CTGAGCCCGT ACCCACACGA CTAGTGATA CAGTTTAAAG GCAAACACTT AACAATGACA 1620
 ATAGTTGGAT AGAGTTTGAA TATAGTCCTG AGCTATTGGT TAGCGTGACC TTTGCTGTCC 1680
 TTAGCATGTG CTGTGAGAAG ATAGAAAAAT GAAGACTTGA GTCTAGTCCT GGAACCCACA 1740
 GAGGCAGGCG AGAACCCACT CCTGAAAGTT GTTCTCTGAG CTTACATAC AACTTCACAT 1800

FIGURE 6A

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AATAGTTACA ATGATAATAA TAATTAGTAA ATTCTTTTAA AAGGTATATG TTGGGAGGGA 1860
GAGATGGCTC AGCTTCCAGG AGCACTTGCT GCTCTGCGAG AGGACCTAGA TTCAGTTCCC 1920
AGGACTCATA TGGTGGCTCA CAGCCATCTG TAAATCCAGT TCCAGAGGGT TCCACACCCT 1980
CTTCTGGCCT CCACAGGCAC CACATACATA GTACACAGAC ATACATGCAG GCAAAAACACC 2040
CATACACACA TAAATAAATA AGGAAACTTA AAAGGTGCAT GTGTTGGTAA ACATTGTGCT 2100
TACACATGCT GATTGAAGAC ATGTACAACG CACACACTGA AGAGGGATCT GGGGCTGGAG 2160
AGATGGCTCA GCGGTTAAGA GCACTGACTG CTCTTCCGAA GGAAGGTCCT GAGTTCAAAT 2220
CCTAGCAACC ACATGGTGGC TCACAACCAT CCATAATGAG ATCTGACACC CTCTTCTGGT 2280
GCATCTGAAG ACAGCTGCAG AGCTACAGTG TACTTAGATA TACTAATAAA TAAATCTTTT 2340
TTTAAAAAAA TGAAGAGGGA TCTGAGACAC CTCAAAAGAG ATTATGAGCA GTGACTCACG 2400
GGTGATTATC TATCCTGGAG TTTTTCCTTT CCGCTTGGCT TGCAACTGGG TGGACAGACG 2460
CCCCTTTTCA TTCACAAGAA CGGGTGCTAC ATTATTTCTG AACAAAACAG CACCTGCAGT 2520
ATGTTTACTG TCCTTGCTGA CTATGAGCAC GCGCACGCGC GCGCGCACAC ACACACACAC 2580
ACACACACAC ACACACACAC ACACACACAC ATTCACTCTC CAGAGCTCTT GGGAAAGGTCA 2640
AGAAGAGGCT GCCCTCAAAC ACGATCTTCA TCTTTCCCTC CTAAAGGAGA CCACGATTCC 2700
AAGGTGGCAG AAGATCTACA GGGGGCAGAG GCAGGGAGGG GGAAGCAGGC CATGGTTTCC 2760
AGAGACCTAC AGCAGAGGGC AGCAAGGCAG ATCCCCAGGT CCAGGGCAGG GAGGTGGAGG 2820
CCCTTGTTCC GAGGAGAAGG CAGGCGGCAG AACAGGGTTC AAAGGCACAG GTTTATGGCA 2880
GCTCATAAAA GTGGAGGTCG TGGCTCACTC AGAAAGGAGG AAGAAGGGAA AGGCCCTTGT 2940
GCCCACTGAG CGAGGGTCAT GCTGAGTAGG AGAGATCTGC AGGGGTGCCA GGAGCCCCAC 3000
CTGTCTGTCC CAAGGGAACC CCAAGTGTGA ACTCTGGCCT TGGGTGCTGA GTTCCAGCTA 3060
CAAGACCCCA GGAGTCCTAC TCCATCCCCA TCCAGTGCCC CCTCGCCCCG CCACACCCCA 3120
CCCCGACTC CCGTGCCACT TCTCTAGGGC TGGAGGGTGG CCAGCCCTGG TGGGGGTTGC 3180
CTACCTGCAG GTAGAGCCCA GGTCTTAGCC GGAAGTGCAC CCCATCCCTG AAGCTGCAGA 3240
GCCAAGGGCG GGGCACACGG CAGCTCAGGC TGTCAGGCTG TTGCTGGGCT CTAGGTTCCC 3300
AGGGACCTGG GCACCTACTT CCCCACCCCC CCATCCATTG TCTCTGGGGC CCTATCTTCC 3360
CTTATATGGT GAAGGAAGTT CCTGGGGGGG GGGGGTGGTG GTGAGGACAA AGGTCGTTCC 3420
GTCTCCTGCA GCCAGCTTGC CACAACCTTC TAAGATCTCC CAGGTGGTGG CTGCCTCTTC 3480

+1

exon 1

(transcription start site)

CAGACAGGTA AGGCAATTGG GTGGGGACAC ATGGTGACCA CAGGTGGTTG GAGGGGACAG 3540
GGTCCTTGCT TCTCTCTGGC AGCCTGTGCT TTCTGTAGCA CCTTGGTATA AGTTTGGGGG 3600

FIGURE 6B

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TGAGGTAAGG TGCTCTGAAA CTCTGAAAGA AGCAAGAAGC CAGCAGGCTG TCTTGGGCCT 3660
TCAATGAAGG AAGTTCACAG ACCCCCTTTC CTGTAAGTCA CCTTCGCTTC ATCTGTGTAG 3720
ATTCCCTGGG ACCAAGGTGG CTCCTGGGAC TCAGATTTCT ACAATTAAAA TCAGGACAGT 3780
CCTGAGACTT GGA CTCCGTG CCTGTATTTA CTACTTCTCT CTGGCTGCTC ATTTCTGTGT 3840
TCATGTCTTA CACATCTGAA ATGGTTTCTT TGTGTCACCA TTCCCCTGAC ACTCCTGGGA 3900
GGTCGTATCC TTGGCACATG TATCCTGGGA TGTAAGCTGC AGCCACCAGG AGAGAGGGGG 3960
AGAGTCAGGA GCTGTGTCCT AGGCCCTATT AGGCCTGGAC ATCACCCCTT TCCTAGAAAT 4020
GGCCCCTCCA TTTTTCGGTT ACCATGATCT ATTTTATATC AGAGTGGGCA GTGAAAGCCA 4080
AACCTGCCCA GAAGTTTGGG ACTCACTCAG ACCAAGGTTA TCTGCTCAGA AATCCCCCTG 4140
TCACTTGAGG TTGGGAGAAT CTGCCTCTGG GGGCTTCCAG GTCTTGGTTA GCAGGAGGGT 4200
ATCCTTTGTA TAGGGCATGA CCTAGTCTAT GGTGTTACTA CATTCTGTGTC CAGTTAAAAG 4260
CTGGAATAA AACCCACGGC AGCGCCAGG ATTCTCTACA GTTGTACCCC AAGAACAACA 4320
AGACAGTAGA TATGCAAGGA TAGGTAGCTG GGGAGAAGAA GAACTTAAAC CCCCCCAAAG 4380
GCCACAGGT TCCGTTCCCT AGTTCACAAT GCCAGTATGA GTGCTAGCTA CTATGGGCTG 4440
TGAGTTGGTA GCTACAAGCA TGAGTGATGT TCATGTGTGT AGTGTGTATA ATCTGAGCAC 4500
TTGGGAGGCT GAAGCAGGAG GATTGCTATA TGTTTGAGGC CAGCCTGAGC TATAGAGCGA 4560
GACTTTGTCT TTAAGAAAAA AATGAAAGCC CAGCAGTGGT GGCACACGCC TTTAATCCCA 4620
GCACTTGGGA GGCAGAAGCA GGCAGATTTT TGAGTTCAAG GCCAGCCTGG TCTATAGAGT 4680
GAGTTCCAGG ACAGCCAGGG CTACACAGAG AAACCTGTGT TTGAAAAACC AGAAAAACAA 4740
AACAAAACAA AACAAAACAA AACCCAAACC CAAACCCAAA CCTCTCATCT CTCATCTCTC 4800
TAGGCTGTGT CTGTCTAGGT GGTAGAGTTT GGGGACTTCA GACTTATATA TAAATAGGCC 4860
TTTTTATCAC TGGTCAGAGA CGAGAAAGGT TTCAGTCTGG GACACAGTGG GACCCTGAGA 4920
AAGTACTCCT TGCCAGCCCA AAAATTCTGG GAAGGCTTCC TGGAGGAAGT GTGTCCCGAT 4980
CAGACTACTG TTCTAGAAGG CAGAAGAGAG GGTGGAAGA ATGTTGGTGG ACAGACAGTT 5040
GGAACAGAAG GACAGGAGGG GGAGGCATCC AAGATTCTGA ACATGTAGCT GACTTTTGGT 5100
TCTCTGGGTG ACAAGTGTCC CCCAGGGATA GGGCTGTAGA AAGGGGACCA GGGGTGAGCC 5160
AATGAGTTCA AGTTGAGGGA CACATCCAGC CCAGGGTCCT TGCTGGCAAG CTAAAGAATG 5220
AGAGCCCTCT AACCTCCCT GAAGTTTAGG GGAGACAGGA GAGCTGAGGA GATCCTTCTA 5280
GGGTGAAGGA GAGGTATCTG CTCTGACCAA CATGGCTAGG AGCAGAAGCA GTTGGACCAG 5340
TTACCCCTCA GAACCAGCCA TCCCCTCTTG GCTCTAAGGA GGCTGGGCCC CTTTCTGTTT 5400
AAGAATCTTA CTTTCTTCA GAGAGAGGCA GCAAGCCTTT GTCCCCTCCC TGTGGTCAA 5460
TAAACACCCC TGTGTGTAAC ATTAGTTTAT TTTACTGTCA GTTGCTCCA GGACAGTCCA 5520

FIGURE 6C

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TCTGGTAGAC CTCTGCTCCT AACTCACCAA GGTATGGCCC ACATTCCTCA CCCAGAAGAG 5580
 TGCAGAAGAG AGCCTTAGAG AAAGGGTAAC AGTAACAAAG ATGGCCAGAA TAAAACAAAA 5640
 ACTACTATCC TTTGTACCCA AATTGGTTTT GCTGAACCAG GAGGGGGTGT GTGAGTGTAT 5700
 GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT 5760
 CTTGGGGGAC TTTTCATGCT AAAGAATATC TGATATTGGC GCCCATGCCA ACAGGGGTAT 5820
 TGGGGAGAGT CAGGCTTCTG CAAACACAGT AAGCTGCCCA AGATGGATTG GTGGCCTGAA 5880
 TCACCAAGGG GCAGGCTGAT CAGAGTGGAC AGAACATCAC AAGATAAGCC ACCCTGTGGG 5940
 GCTCAGAAGA GGGAGTTTAC AAGAGGTAAA GGCCAAGCCA TTTATTATCC AAGACATGAC 6000
 TCAAAATCAA AGTGCAAGGA GAGATTAGCT GGAGAGATGG GGCTGTCAGT GTGGGACACC 6060
 TGACCTTGCA CTTATTAGTC ACTAGGCCAA GGAGCAGTCA CAGAGGGTGA CTGGGTCCTA 6120
 CTCAGCTTGG AGCAGGCACG TGGAGAATGG GTGACCTCCA TCCTGATGGA GAGGGCTGAG 6180
 CACCACCAGG TACAAGTGTT CCCTGTGTCT CATGCCAGGA TTCCTGGCCA GTTTTCAAAG 6240
 GACTAAGGAC TCATCTCTGG TGGAAACAAA GTATCCAAGC CCTAAGCCCC ATTTTGGTCT 6300
 AATTAAATCA GAACCCCTGG GGATGCAGGC TCTGAGCAGC AGGAGCTTTT TAAAAAGCTC 6360
 CCAGGTGATT CTGATCAGCA GCTGGAACAA ACACAGCTAC AGGTTCAAAC AGAAAGAGGC 6420
 AAAGCTAGGG AAAGCTTGGG ATGGGGAGCC TTCTTCCAGG CCAGTAGATG GAGGCTGGTT 6480
 AGCAGTGGTG GCAGCTTCTC TCTGCCTGTC ATATAGCTAT CCATCCACTC ATCCATCCAT 6540
 ACACCCACCC ATCCATTTAT GCACCCATCC TTCCATCCAT CCATCTATCC AGCTACCCAC 6600
 CCACGCATCC ATCCAAACCT TCCTTTTCTC CTTCTTTCTT TCTTTTTCCT TTTACTCATT 6660
 CATTTATCCA ACAGAGAACT GGTATTGTAC TAAATGTGGG AGATTTAATT AATTTTTAGA 6720
 AGCTCTGTTG ATTGACTGAT TGTGCATGTA TGTGGACAGG TACATACCAC AGCACACGTG 6780
 TGGCAATCGG AGAAAGGTTT TGGGTGTTGT TTTCTCTTCC CACCGTGTGG GTTCTGGGGA 6840
 TTGAACTCAA ATTATCGGGC TGGTGGCAAG TGTCTTTACC ACCGAGCCAT TTTGCTGACA 6900
 CATCATTATT ATTAGAAAGC ATCTTATGTA GTCCAGGCTG GCCTCAAGCT TGCTATGTCG 6960
 CCACGGATGA CCTTTAACTC CTGCTCTTCC AGCCTCCACC CGAGTGCTAG GTTTACAGGT 7020
 GTTCAACTGG TGAATGCCTT TAATCCCAGC ACTCTGTGGG GGGGGGGGGG GAGGCGGATC 7080
 CCTGAGTTGG AGGCCAGTTT GGTCTACAGA GTTTCAGGAT ACCTGGGGCT ATACAGGGAA 7140
 ACCCTATCCC AAACAAACAA ACAAACAAAC AAAAAATATT CTGTGCAATA ATCACAGAGA 7200
 TTAGAGGATA TTAGTAGGGT AGTAGGGCTG GTGAGGGAGA GTCATGCTTT CTTTTGTATT 7260
 ATAATAGTAA AGTACTACA AGATGCATTA TCTATCTATC TATCTATCTA TCTATCTATC 7320
 TATCTATCTA TCTACCTACC TACCTACCTA TCCATCCATC CATCTATCGT ATAGCCCAGG 7380
 CTGCTTTGAC TCTGAATGCT CCTATTTCTG GGTCAACTCT TCACCCCTAG TGTGGGTTT 7440

FIGURE 6D

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ACCAACACCC AGACATTTAT TTTATTTTGT TTTATTTTAT TAATCTAGGA GCTCAGGGTG 7500
GGACTCAGGG TCTTGTGCAT GCTAAGCAAG CTCTCTGCCA CAGAGCTGCA GCTCCAGTCC 7560
CCATTTTGTT CAGGTGACTC TGTGACAGTT GTCATATTCG CAGCGCTATG TAGCTCTCTC 7620
CACCTCCCAG TTCCAGCACT TTCTGGTCAT CCCAGTGGGC GGGCAACTCT GTGCTCACCA 7680
GTGCCCTGTT CCCTGTCTTC AGACCTACAT ATTTGCCTGT CTGAACAGTT CATGTAAATG 7740
GGATGCGTTC CTGTGTATTC TTTTATGGCT GGCCCCTTTA TCTTAGCACA GTTTGTGTTG 7800
GGCCATGTGT CACTGCTATA CTCTATCTTA TCATCATCTT ATGGCTTAAT AGTGTTCCCT 7860
TGTGTGGATA AACCACTTTC TGTTTCATTT ACTGATGGAA ATTTGTGGCC CCACCCCCAC 7920
CCTTTTTTTT TTTATTTGAG ACAAGGTCTT TCTGTGTAAT CTTGCAATCT TGGCTGTCCT 7980
GAGCTCACTC TGTAGACCAG GCTGTGAGGC TGTCTTCCA CTTTTGACAC TCCTGTGAAC 8040
AGAGTAGCCA TGAACCTCAA AGACAATTTT CTGTTTTGGT TTGTTTTTTA CATTTGTGTG 8100
TGTATGCGTG TATATGTGCA TGTTTGTGTC TTCAGGTGCT CACATGTGTG TACCTGTGTG 8160
TGGGACAGAG AACAAACCGA TGTGCCATTC CTCAGATACT ACGCATCTTG TTAATATGTA 8220
TGTATTATGT ATGTTTATTT AGTGTGCCCA AGTATGCAGG TATTTTGTG GAGTTTTCAC 8280
CTTCCCTTGT GGGCTCTCCG CATTAAACTC AGCTCCTCGG GCTAGTGAGC AATGCCCTCA 8340
CTCGATGAGC CATCTCGCTG CCCCTGCTGC CACCTCCTCC TTATTTCCCA GATGGGACTA 8400
CGCACTGCAC TGGCCTAAAG CTCACCAAGT CATCCAGAGT GGCTAGCCAG GGAGACTCAG 8460
GGATATGCTG GCCTCTGCCT CCACAGTGCT AGAATTACAG GCATACATCA CTGCTGGAAG 8520
ATTTTTAACC TGAATCCTGA GGATAGAGCA GGCACCTCTAC CAATGGAGGG TTCTTTTTGT 8580
GTTTGGTTTG GTTTCCTCTG CATAAGATCA GGCAGTCTGA AATAGTGTAG CCTGGGCTAC 8640
ATAACATCTT GTCTCAAAAA GCCTATAGAG GTAGGGAGGT CGAGGCTAAA GAAGAGCCTT 8700
AAGCCGGCTG TGATAGCACA CAGGATAGCC TGCATATAT AGCAAGACCT TGTTTCAAAA 8760
ACATGGAGGG AGGGGTATGT TTTAAGTGCT GGGCTGTGTA ACAGGCACTA AGGGAGCCAA 8820
TGTAGACATT TGACTAAGAA AGGATCATCA TCAAAGCCGG GTGGGCAGGG TAGAGGTTGG 8880
ACTACAGTGG TCAAGACCCC CATAGGAAGC CAGTTTCCCT TCTTCCTCTG GGCCTCAAGC 8940
CTGGCTCGAC GGCCACTGCT CTCACATGCC TTCTCCTCTA GGCTCGTCCA CCATG 8995

exon 2

FIGURE 6E

Targeting using the regulatory sequences of the mouse villin gene Data obtained by transgenesis - October 1998

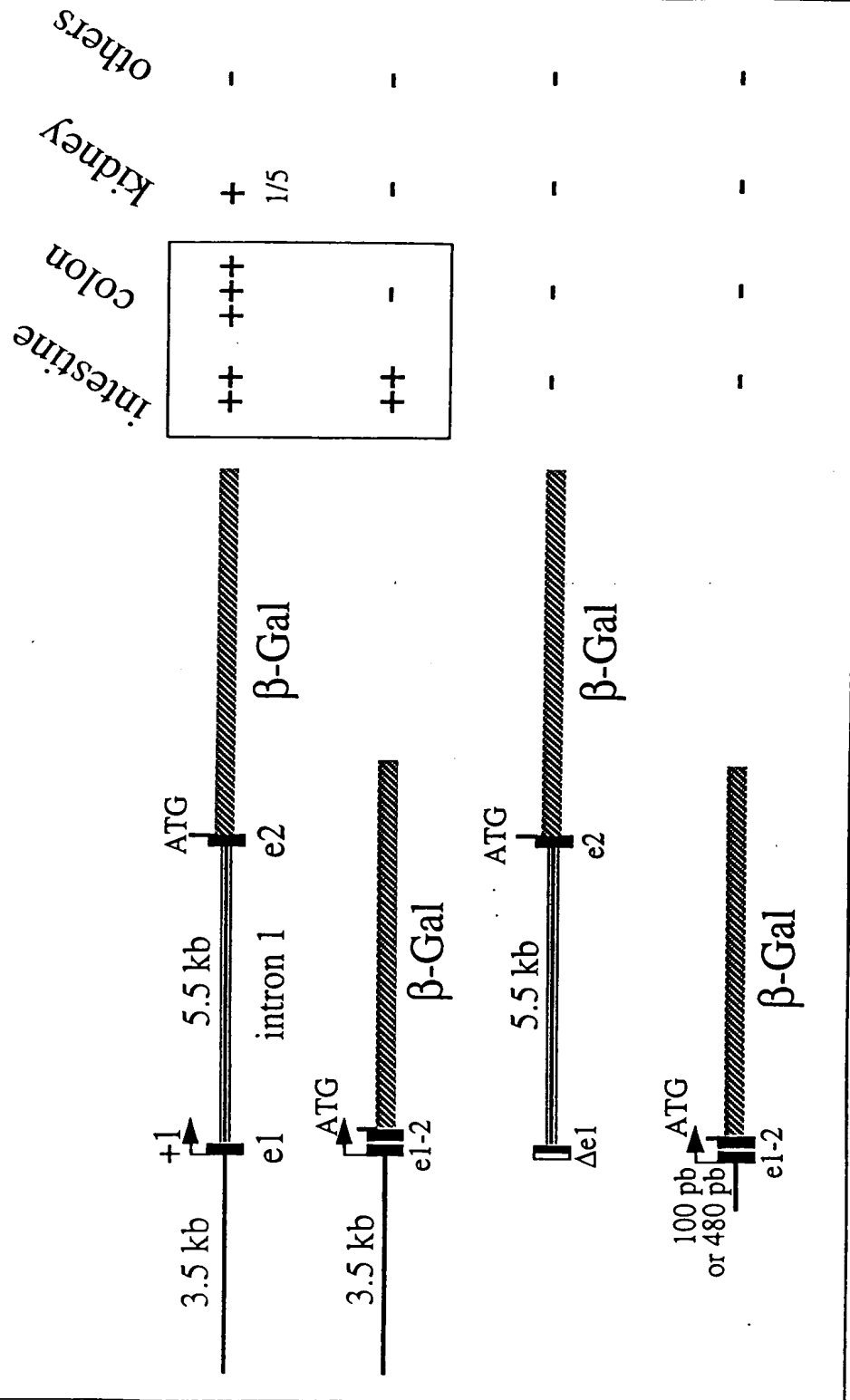


Figure 7

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Targeting of oncogenes and tumor suppressor genes

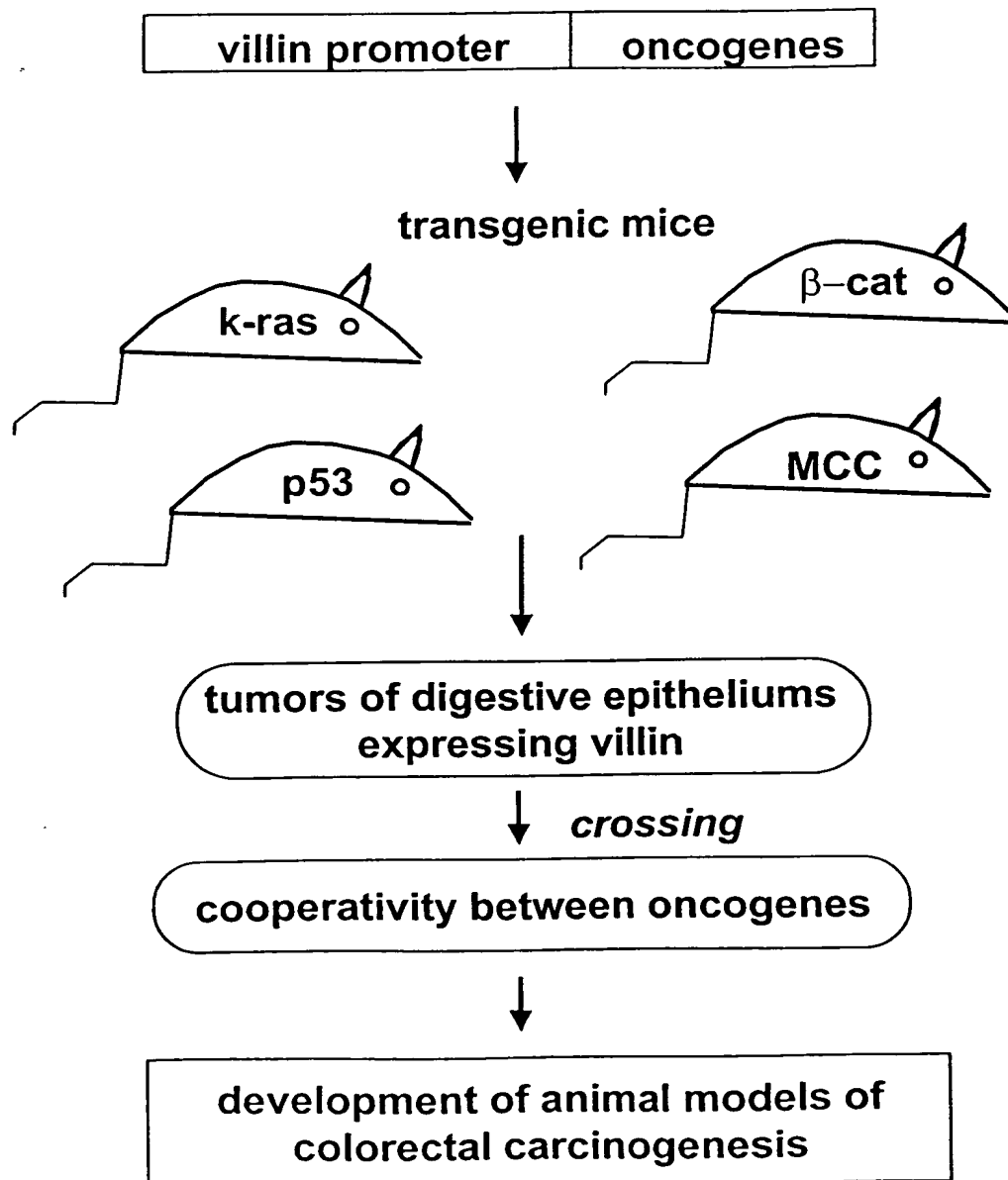


FIGURE 8A

Targeting of immortalizing gene

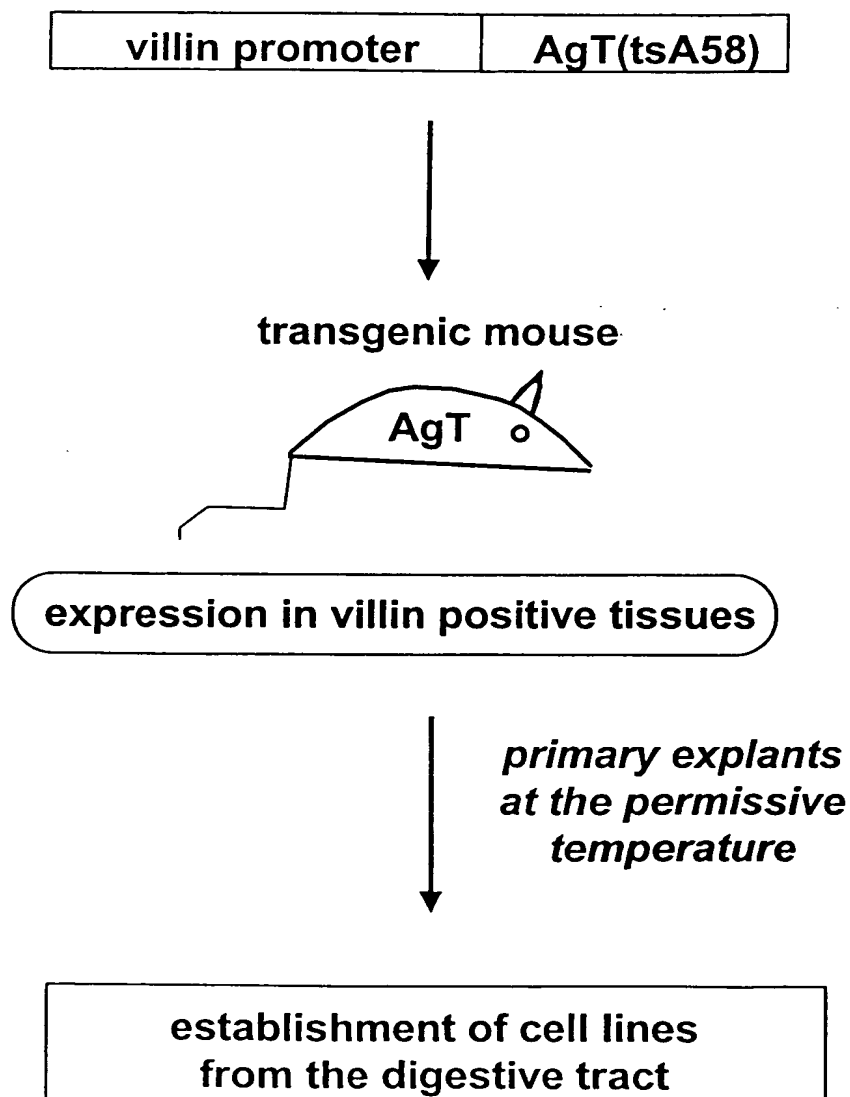


FIGURE 8B

Targeting of transactivator gene (repressor form rtTA)

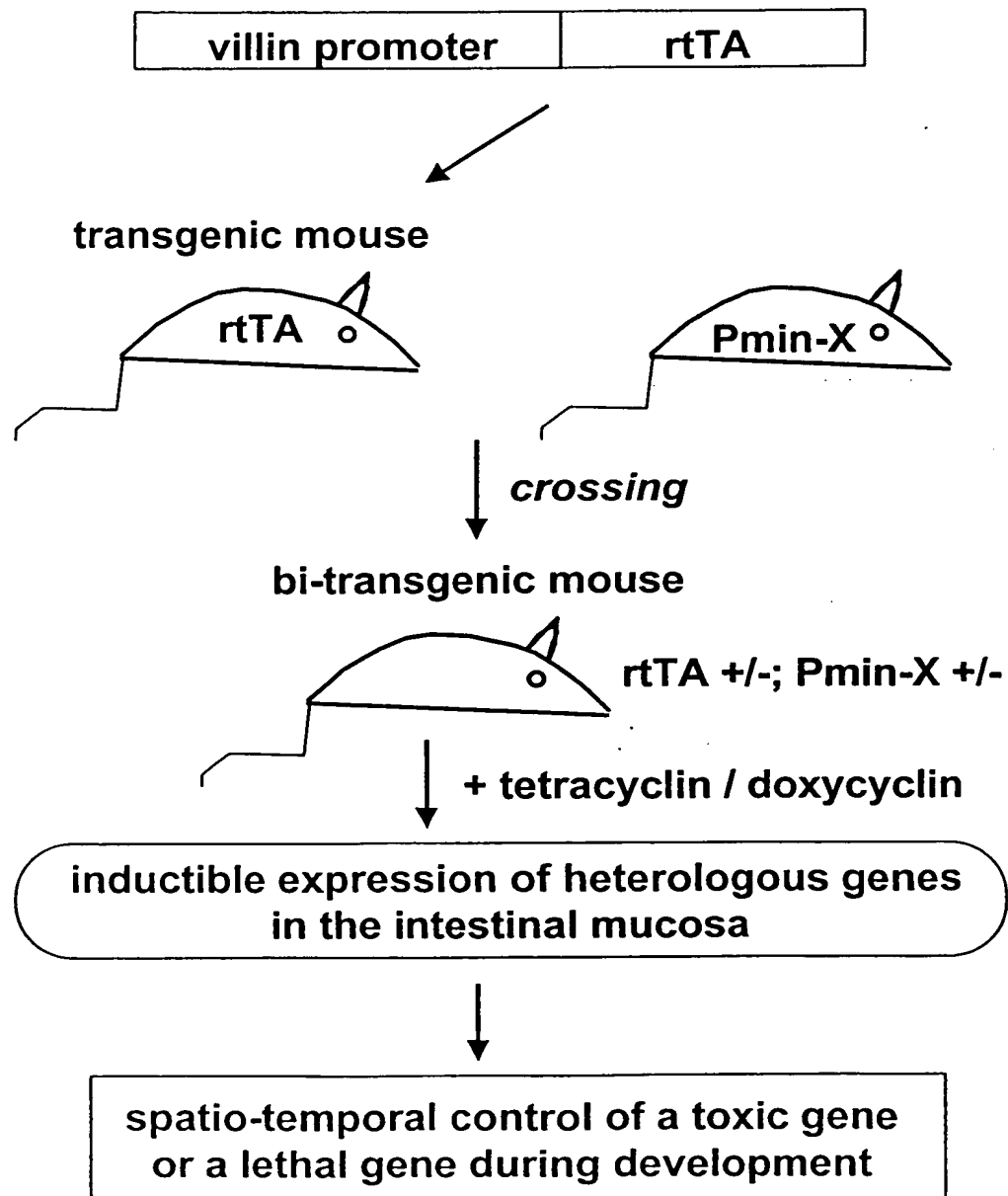


FIGURE 8C

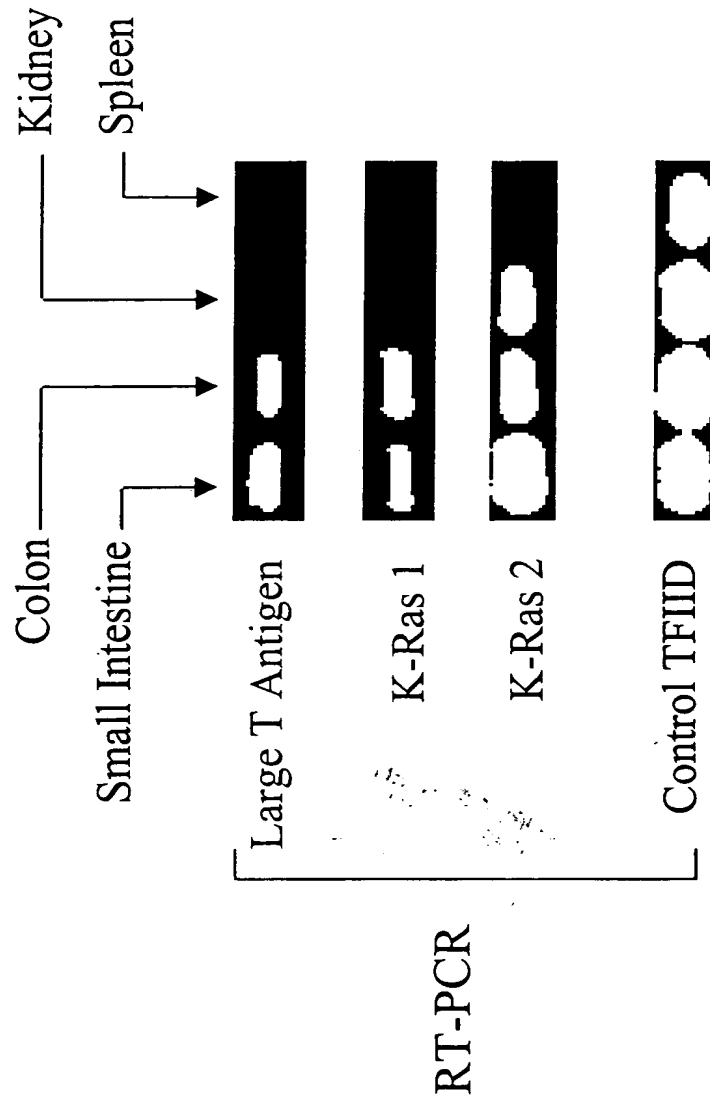


FIGURE 9